REMARKS

The specification has been amended to remove possible hyperlinks and to correct typographical errors

Claims 3-8 and 27-42 have been canceled as being directed to a non-elected invention.

Claims 21 and 23 have been canceled.

Claims 1 and 2 have been amended so as to be limited to the elected species, S3.2, SEQ ID NO:211. Claim 9 has been amended so as to be limited to the elected propeptide, SEQ ID NO:210. Claims 10 and 24 have been amended to correct typographical errors. Claim 10 has further been amended to limit the voltage-gated ion channels to voltage-gated neuronal sodium channels. Support for this limitation can be found at page 3, lines 30-32 and in Example 8 on page 89 of the specification. Claim 19 has been amended to more clearly claim the pain type or pain associated with certain disorders. Claim 22 has been amended to depend from claim 10.

It is submitted that none of these amendments constitute new matter, and their entry is requested.

On page 3 of the Office Action, the Examiner indicated that claims 3-9 and 27-42 were withdrawn from consideration as being directed to a non-elected invention. However, Applicants submit that claim 9 was improperly withdrawn as the Examiner stated in the Office Action mailed 30 September 2002 that she would search the propeptide along with the mature toxin. Applicants identified claim 9 as reading on the S3.2 propeptide in the Response to Restriction Requirement filed 24 December 2002. In addition, Applicants note that the Examiner indicates in the present Office Action that the propeptide and the native peptide are free of the prior art. Applicants request that claim 9 be included in the examination of this application.

In view of the objection to the Declaration and Power of Attorney, Applicants are submitting herewith a fresh Declaration and Power of Attorney executed by Gregory Shen, the inventor who had made changes in the previous declaration without initialing them.

Applicants note the Examiner's comments concerning Table 1. However, Applicants believe that the sequences in Table 1 are appropriate since the Xaa1, Xaa2, Xaa3, Xaa4 and Xaa5 designations are generic variables as specified in Table 1 and do not make reference to an amino acid

position. The sequences set forth in the Sequence Listing make reference to the position of these variables within the amino acid sequence of the peptide.

The specification has been amended to address the remaining objections noted on page 4 of the Office Action.

The claims have been amended to address the objections noted on page 5 of the Office Action.

Claims 10-26 were rejected under 35 USC §112, first paragraph, for lack of written description and for lack of enablement. The essence of the Examiner's rejection is that "there is no evidence of record to show the specificity of this conotoxin [S3.2]; as such, the contribution of the specific channel to each of the recited disorders cannot be determined." It is submitted that the Examiner is in error in these rejections.

The specification discloses that the disclosed peptides, including conotoxin S3.2, are μ-conotoxins. It was well known at the time of the present invention, and described in the present specification, that μ-conotoxins are selective for voltage-gated sodium channels. This knowledge is further shown by McIntosh et al. (*Meth Enzymol* **294**:605-624, 1999). To support the conclusions made in the Office Action, the Examiner refers to page 606 of McIntosh et al., where it discusses the major interest of conotoxins to neurobiologists. This passage, especially in context with the entire article, demonstrates that the various classes of conotoxins, such as α-contoxins, μ-contoxins and ω-contoxins, have different subtype-specific activity. (This activity of the different classes of conotoxins is also described at pages 2-3 of the specification.) However, McIntosh et al. teaches that the μ-conotoxins are sodium channel blockers, competing with saxitoxin and terodotoxin for site 1. See Table 1, page 607. See also the discussion at pages 618-619 which further describes this activity of the μ-conotoxins. The present specification describes (a) the peptide S3.2, (b) peptide S3.2 as a μ-contoxin, and (c) the fact that μ-conotoxins, including μ-conotoxin S3.2, are specific for voltage-gated sodium channels. Claim 1 has been amended to specify the ion channel as a neuronal sodium channel. The specification further describes conditions and disorders which can be treated with μ-conotoxins having specificity to sodium channels. See, for example, page 3, line 32 - page 4, line 3 and page 6, line 10 - page 7, line 7. The Examiner has not provided any scientific evidence or

reasoning to conclude that peptide S3.2 is not a μ-conotoxin and that it does not have activity at voltage-gated sodium channels, as described in the specification. Thus, the specification clearly demonstrates that Applicants were in possession of the claimed invention.

Furthermore, the Examiner is incorrect in her assertion that there is no evidence of record showing the specificity of conotoxin S3.2. Example 8, found on page 89 of the specification, shows that conotoxin S3.2 acts on sodium channels and is particularly selective for neuronal sodium channels. The Examiner has not provided any scientific evidence or reasons to doubt this teaching concerning the activity of μ-conotoxin S3.2.

Thus, in view of the above remarks, it is submitted that the amended claims are adequately described and enabled by the specification. Withdrawal of these rejections is requested.

In view of the above amendments and remarks, it is submitted that the present claims satisfy the requirements of the patent statutes and are patentable over the prior art. Reconsideration and early notice of allowance are requested. The Examiner is invited to telephone the undersigned in order to expedite prosecution of the present application.

<table>
<tr><td colspan="6">RESPECTFULLY SUBMITTED,</td></tr>
<tr><td>Name and Reg. Number</td><td colspan="5">Jeffrey L. Ihnen, Registration No. 28,957</td></tr>
<tr><td>Signature</td><td colspan="2">  </td><td>Date</td><td colspan="2">12 September 2003</td></tr>
<tr><td>Address</td><td colspan="5">Rothwell, Figg, Ernst & Manbeck, pc
Suite 800, 1425 K Street, N.W.</td></tr>
<tr><td>City</td><td>Washington</td><td>State</td><td>D.C.</td><td>Zip Code</td><td>20005</td></tr>
<tr><td>Country</td><td>U.S.A.</td><td>Telephone</td><td>202-783-6040</td><td>Fax</td><td>202-783-6031</td></tr>
</table>